Peng, Kuo-Liang

From: Patricia Folkins [pfolkins@bereskinparr.com]
Sent: Thursday, December 14, 2006 4:36 PM
To: Peng, Kuo-Liang
Cc: Lisa Leclerc
Subject: Re: US Patent Application S.N. 10/814,123, Our ref. 3244-126
Importance: High

Dear Examiner Peng,

As per our recent telephone discussion regarding the above referenced patent application, attached please find an electronic version of Exhibit C.

Please contact me if you have any questions and, if possible, please confirm receipt of this e-mail.

Thank you and best regards,
Patricia

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EXHIBIT C

Evidence is provided below to demonstrate that DGS ≠ TEOS; DGS ≠ TEOS + glycerol; DGS ≠ PGS; DGS ≠ PGS + glycerol. In all cases, a head-to-head experiment was run using PEO of 10K MW. The experimental procedures are shown below.

As can be seen from the attached scanning electron microscopy (SEM) pictures, the DGS samples 1, 5, 6 exhibit macroporosity and (not shown) mesoporosity. The morphology of the structures varies, but is in all cases open. Sample 2 is not macroporous. Under these conditions, the gelation occured prior to phase separation. In order to slow down gelation, one equivalent of glycerol was added while other conditions were kept constant. The retarded hydrolysis rate led phase separation occurring *prior* to gelation and a macroporous structure was achieved (sample 6). To more broadly show the effect of changing the rate, 1 equiv. of glycerol was added to all of DGS, TEOS and PGS systems (samples 5, 6, 7, 8 11 and 12). As can be clearly seen, under these conditions only DGS at either pH 5.5 or pH 11 led to macroporous structures, while TEOS and PGS did not.

The SEM pictures of TEOS derived silica show that macroporous structures are not formed: with glycerol present, a 2 phase system results that does not cure within 1 day.

PGS does not lead to macroporous silica, irrespective of the presence of glycerol.

Procedure: Sample **1**: **DGS** (1.00 g, 4.71 mmol) was dissolved in H_20 (1000 µL) at 0 °C with sonication for 20 min. An aqueous solution of HEPES buffer (1000 µL) at 50 mM, pH 5.5 (sample **1**) (or pH 11 (sample **2**)) containing 16% PEO (MW=10,000) (w/v) was added and mixed. The mixture was allowed to stand at room temperature to gel. Phase separation and gelation occurred after 2 min (sample **1**) and 3 min (sample **2**), respectively, to give an opaque hydrogel. The gel was aged at 4 °C overnight, followed by aging at room temperature for 2 days. After washing with H_2O (each time 10 mL x 5 times), and drying in air at room temperature for 1 week, an opaque xerogel was obtained. Samples **2** (pH 11), **5** and **6** were prepared similar to sample **1**, reaction conditions are listed in Table 1. For **5** and **6**, 1 equivalent of glycerol (to DGS) was added to DGS aqueous solution.

Sample **3**: **TEOS** (0.98 g, 4.71 mmol) was mixed with H_2O (1000 µL) and sonicated at 0 °C for 20 min. An aqueous solution of HEPES buffer (1000 µL) at 50 mM, pH 5.5 (sample **3**, pH 11, sample **4**) containing 16% PEO (MW=10,000) (w/v) was added and stirred at room temperature for another 20 min. The mixture was allowed to stand at room temperature for 30 min, two solution layers formed and after 1 day there was a small amount of white solid precipitate which was collected by centrifugation, washed with H_2O and dried in air. Samples **4**, **7** and **8** were prepared similar to sample **1**, reaction conditions are listed in Table 1. For **7** and **8**, 1 equivalent of glycerol (to TEOS) was added. In sample **4**, a very small amount of white precipitate formed in the interface of two layers after standing at room temperature for 1 day, which was collected by centrifugation, washed with H_2O and dried in air.

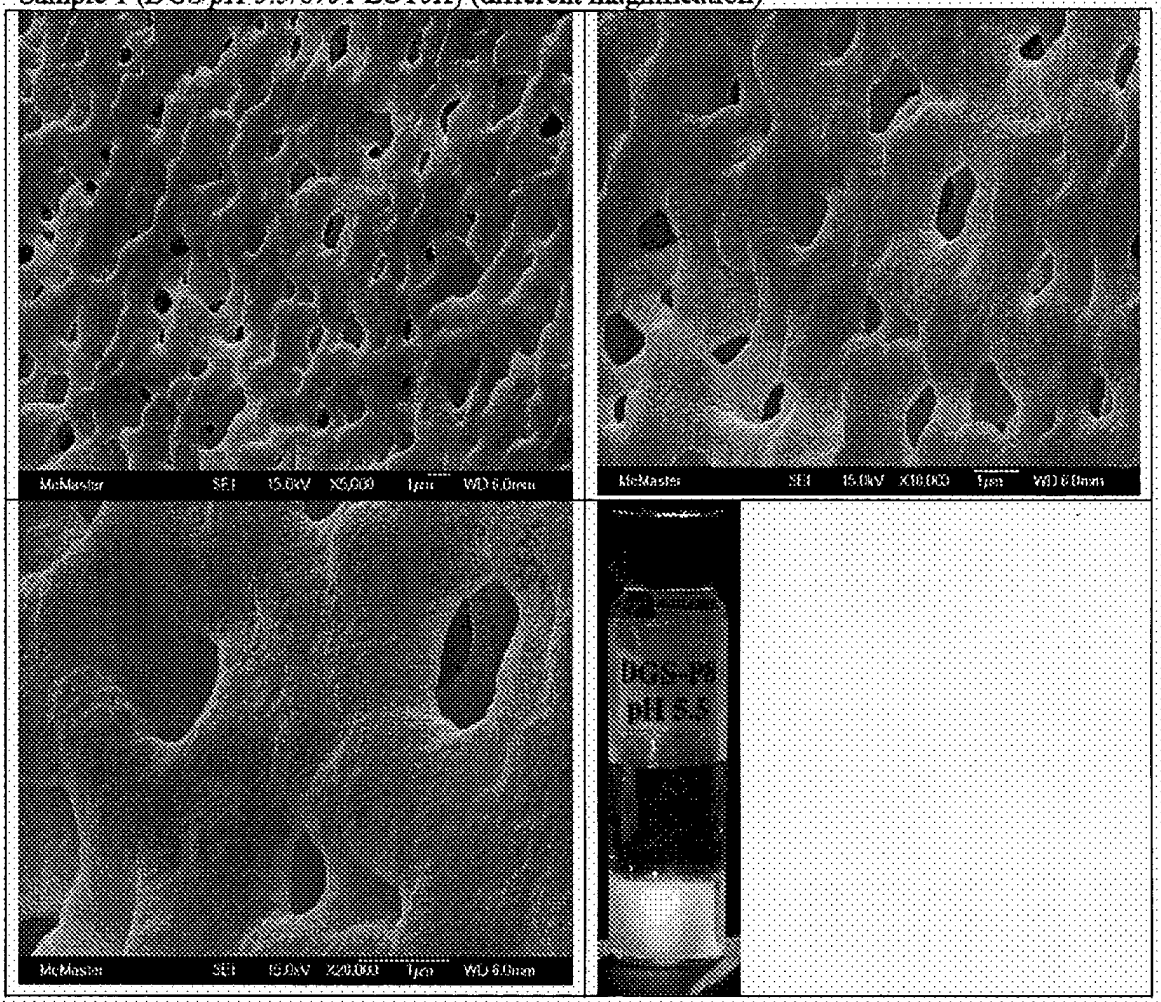
Samples **9** and **10**: **PGS** was prepared according to the literature (Gill, J. Am. Chem. Soc. 1998, 120, 8587-8598). It was found that PGS is not fully soluble in H_2O. The mixture of PGS (5.00 g) and H_2O (5000 μL) was sonicated at 0 °C for 20 min, and filtered; an insoluble solid (1.17 g) remained. In order to keep the ratio of Si:H_2O:PEO consistent with the DGS and TEOS system, to the filtrate was added H_2O (1420 μL). Thus, this prehydrolyzed PGS solution contained 0.6 g (4.71) mmol of PGS in 1000 μL H_2O. Sample **9** and **10** then were prepared similar to sample **1** and **2**, reaction conditions are listed in Table 1. For 11 and 12, 1 equivalent of glycerol (to PGS) was added to the PGS aqueous solution.

Table 1. Reaction condition for preparation of silica monolith.

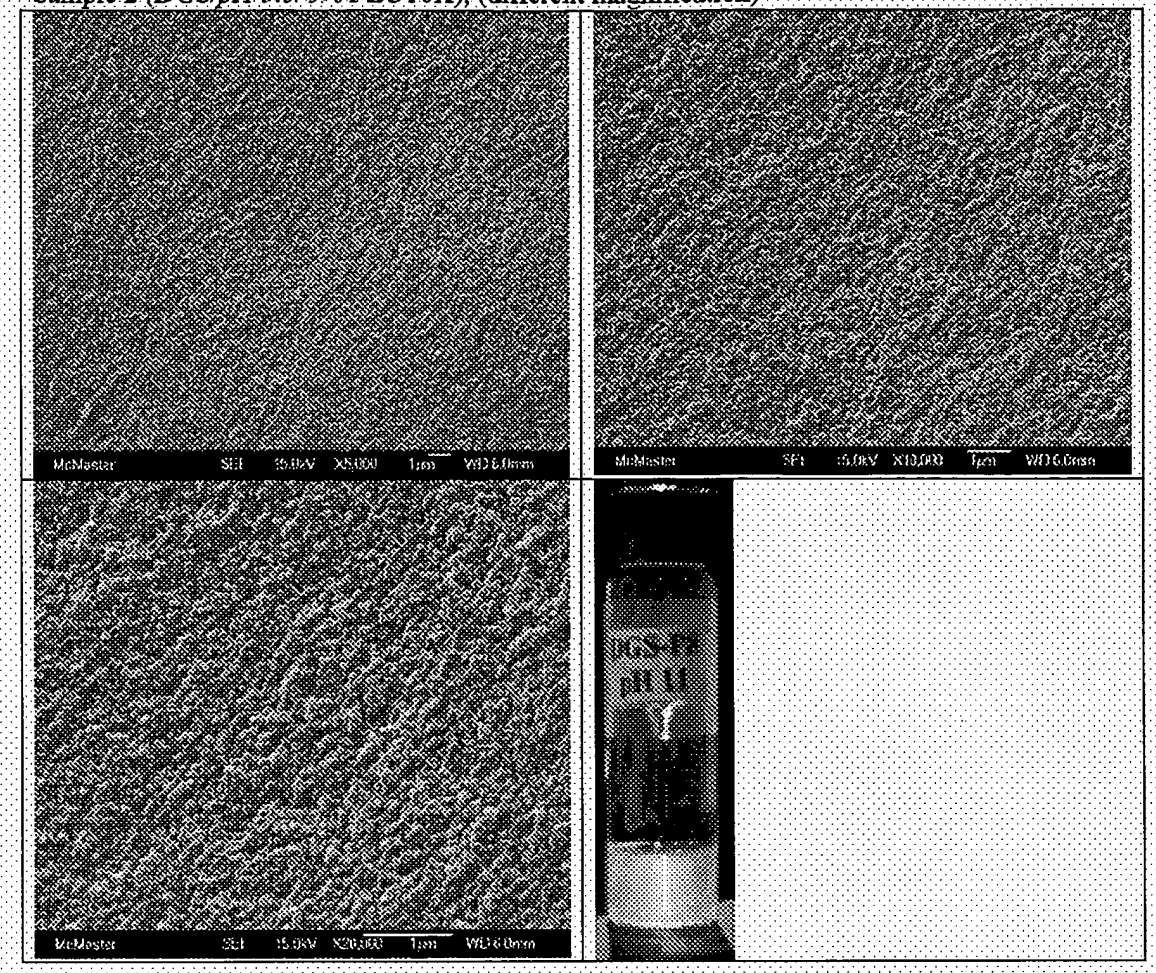
Sample	DGS, g (mmol)	TEOS, g (mmol)	PGS G(mmol)	Additional glycerol g(mmol)	HEPES buffer (original 50mM), containing 16% w/v, PEO-10K	
					pH 5.5	pH 11
1	1.00 (4.71)				1 mL	
2	1.00 (4.71)					1 mL
3		0.98 (4.71)			1 mL	
4		0.98 (4.71)				1 mL
5	1.00 (4.71)			0.433(4.71)	1 mL	
6	1.00 (4.71)			0.433(4.71)		1 mL
7		0.98 (4.71)		0.433(4.71)	1 mL	
8		0.98 (4.71)		0.433(4.71)		1 mL
9			0.60 (4.71)		1 mL	
10			0.60 (4.71)			1 mL
11			0.60 (4.71)	0.433(4.71)	1 mL	
12			0.60 (4.71)	0.433(4.71)		1 mL

SEM images

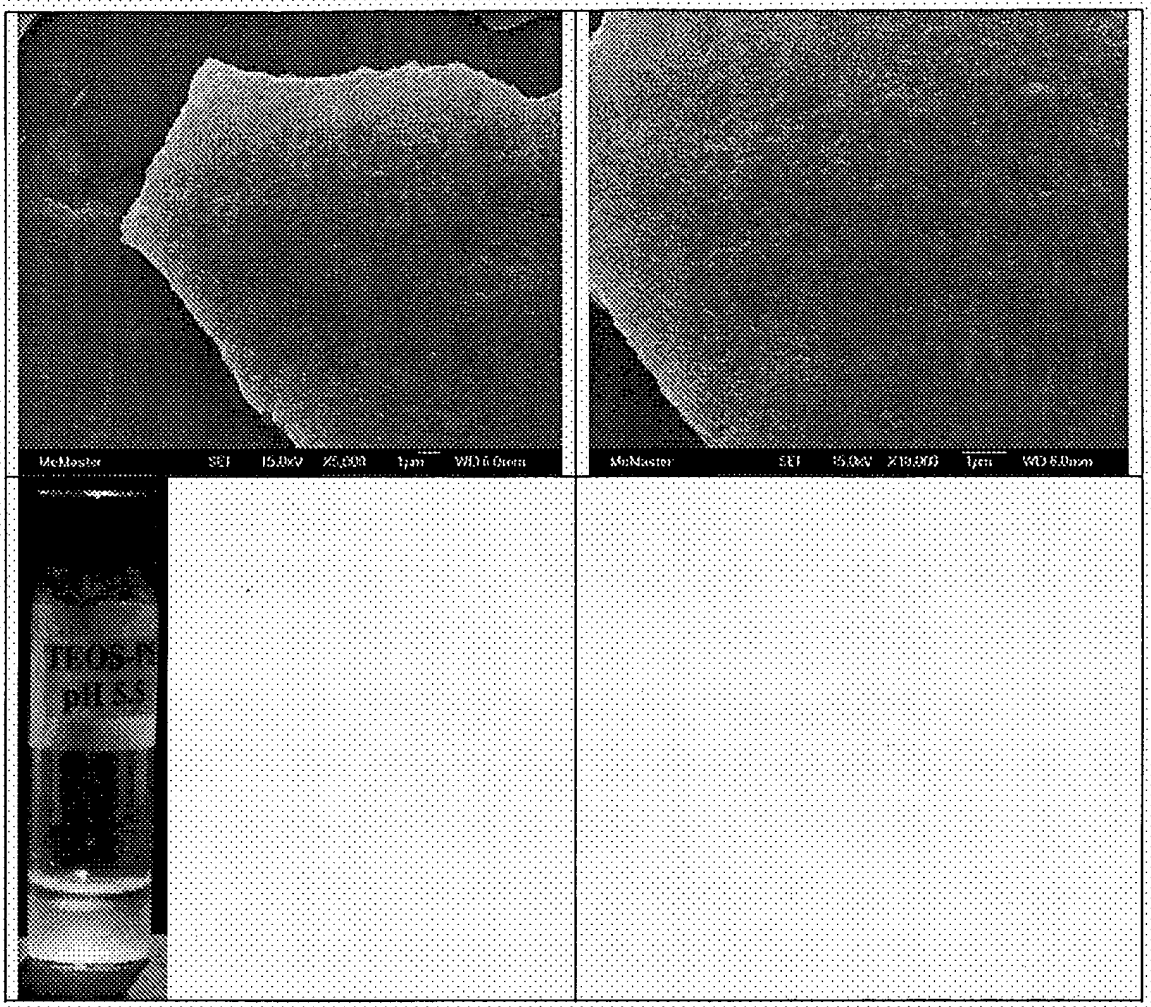
Sample 1 (*DGS/pH 5.5/8% PEO10K*) (different magnification)



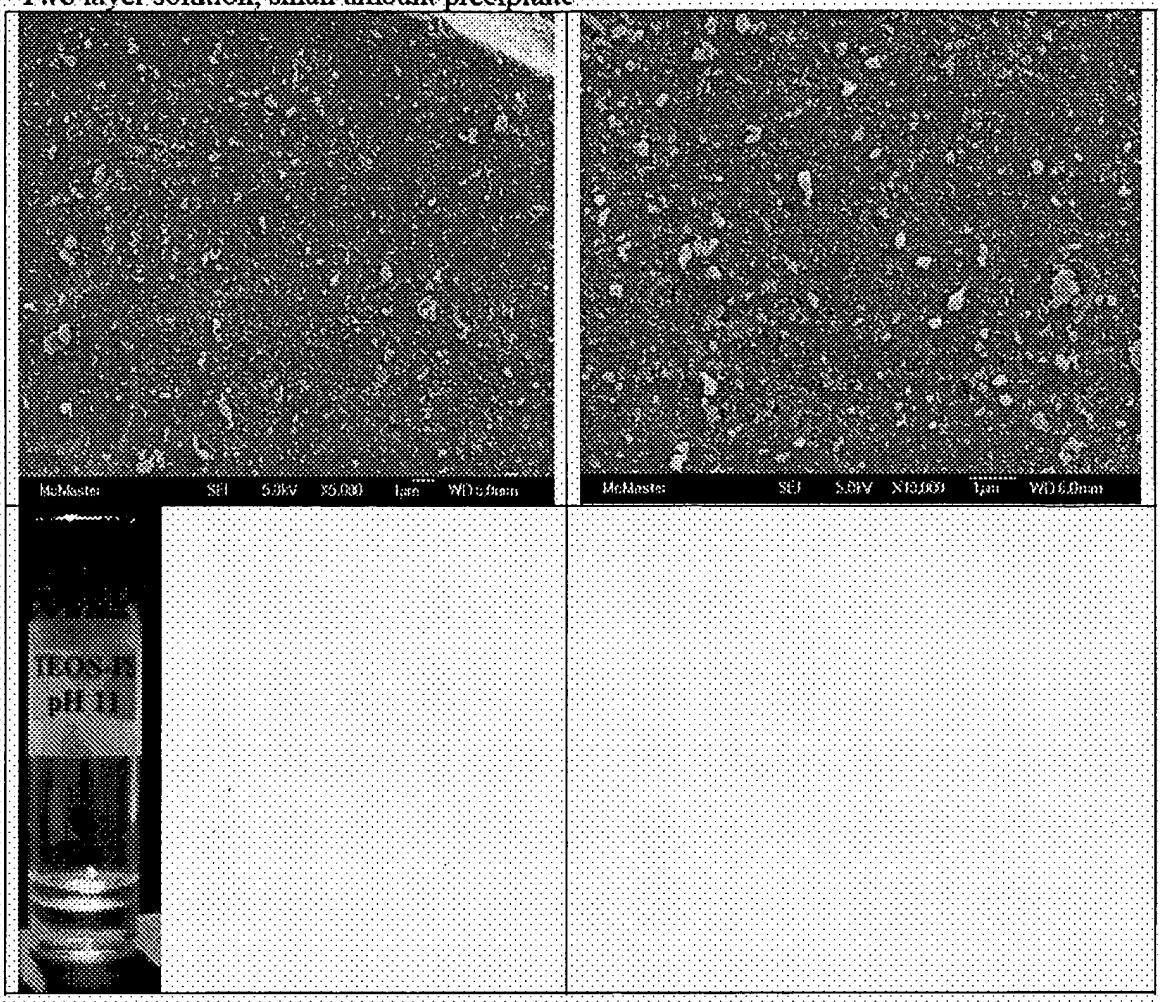
Sample 2 (*DGS/pH 5.5/8% PEO10K*), (different magnification)



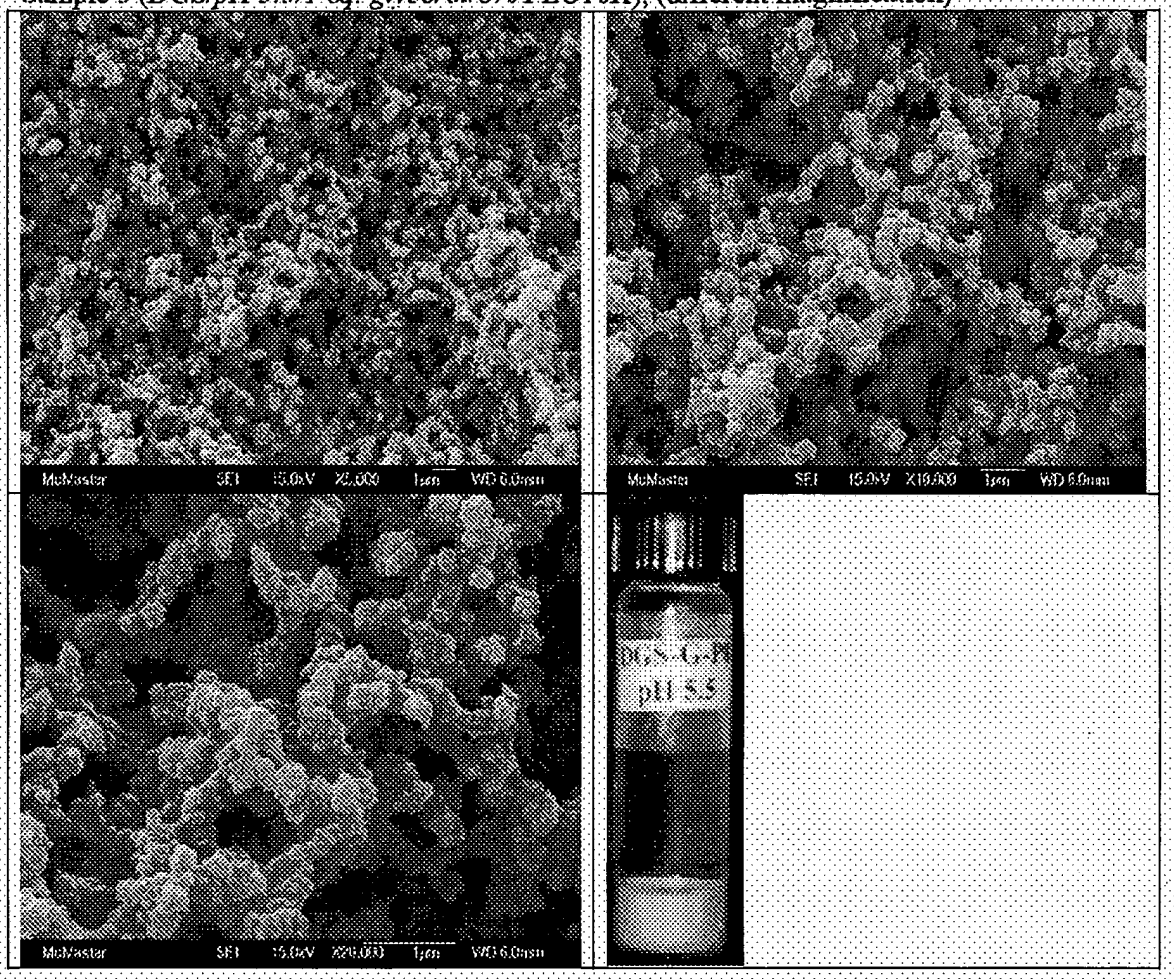
Sample 3 (*TEOS/pH 5.5/8% PEO10K*), (different magnification)
Two layer solution, small amount precipitate



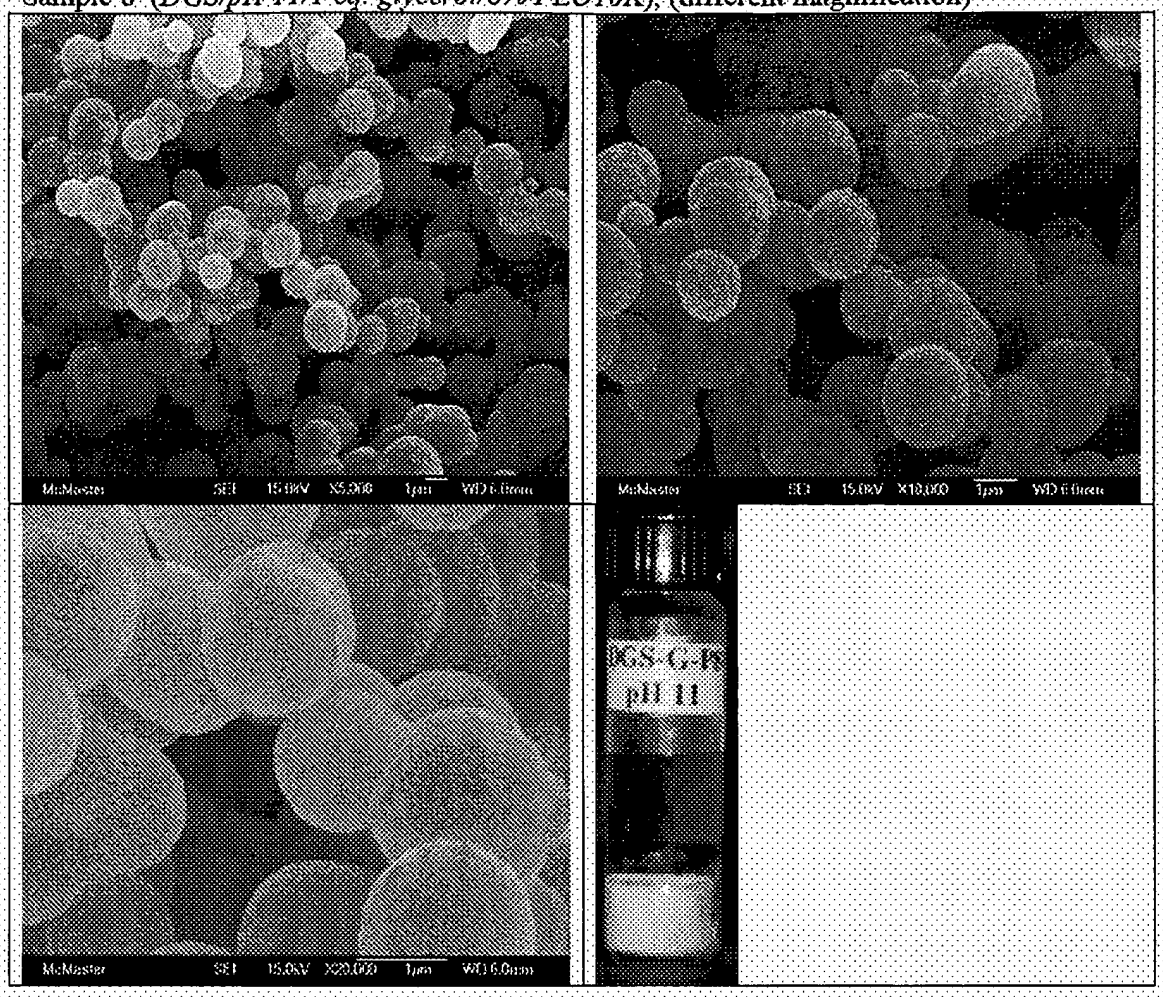
Sample 4 (*TEOS/pH 11/8% PEO10K*), (different magnification)
Two layer solution, small amount precipitate



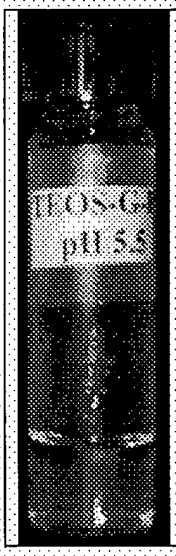
Sample 5 (*DGS/pH 5.5/1 eq. glycerol/8% PEO10K*), (different magnification)



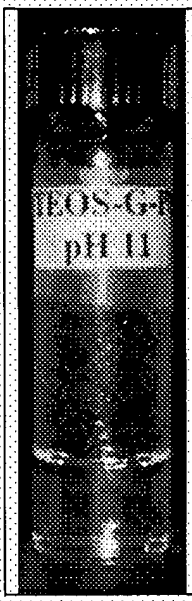
Sample 6 (*DGS/pH 11/1 eq. glycerol/8% PEO10K*), (different magnification)



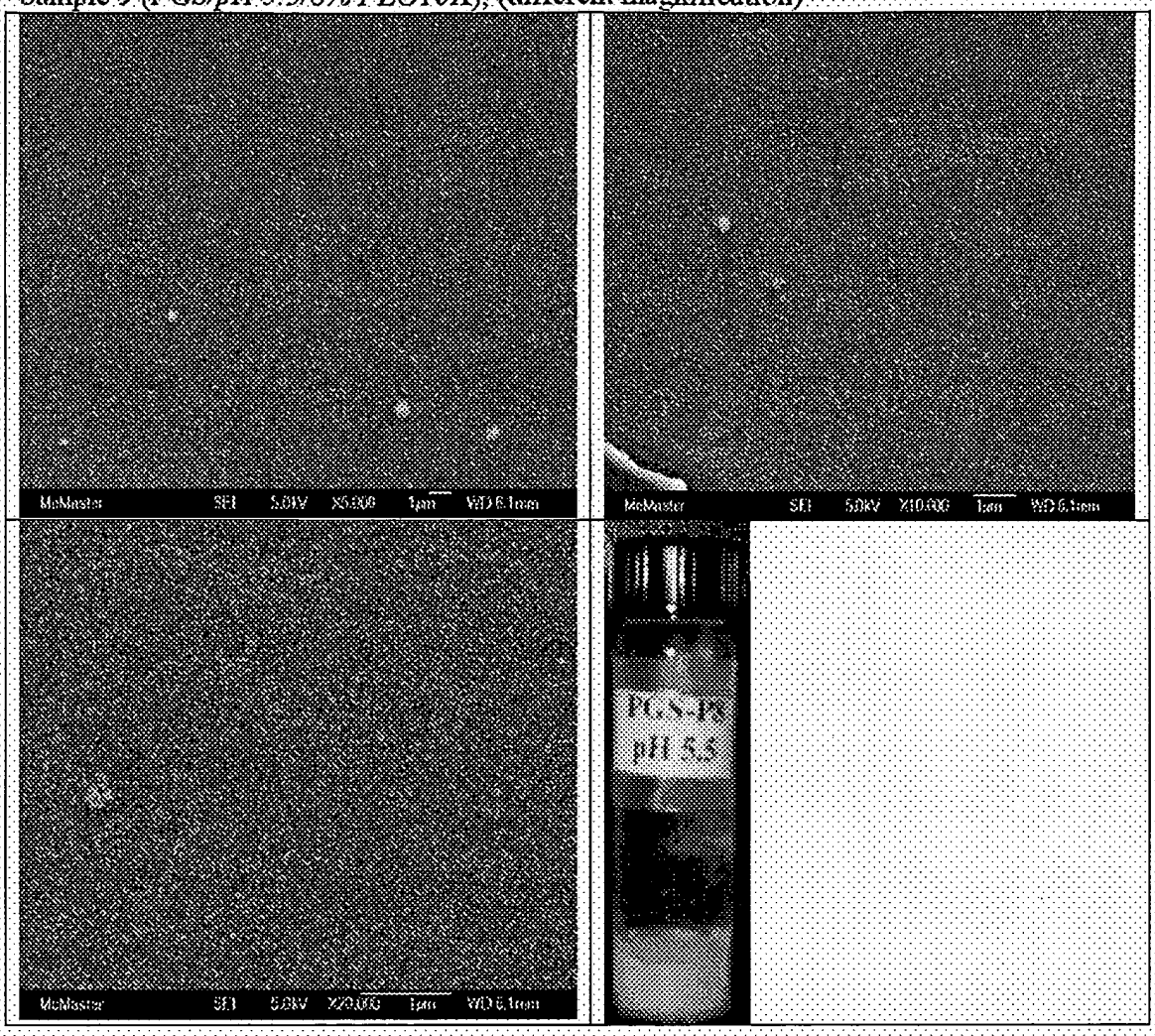
Sample 7 (*TEOS/pH 5.5/1 eq. glycerol/8% PEO10K*), Two layer solution, SEM is not available

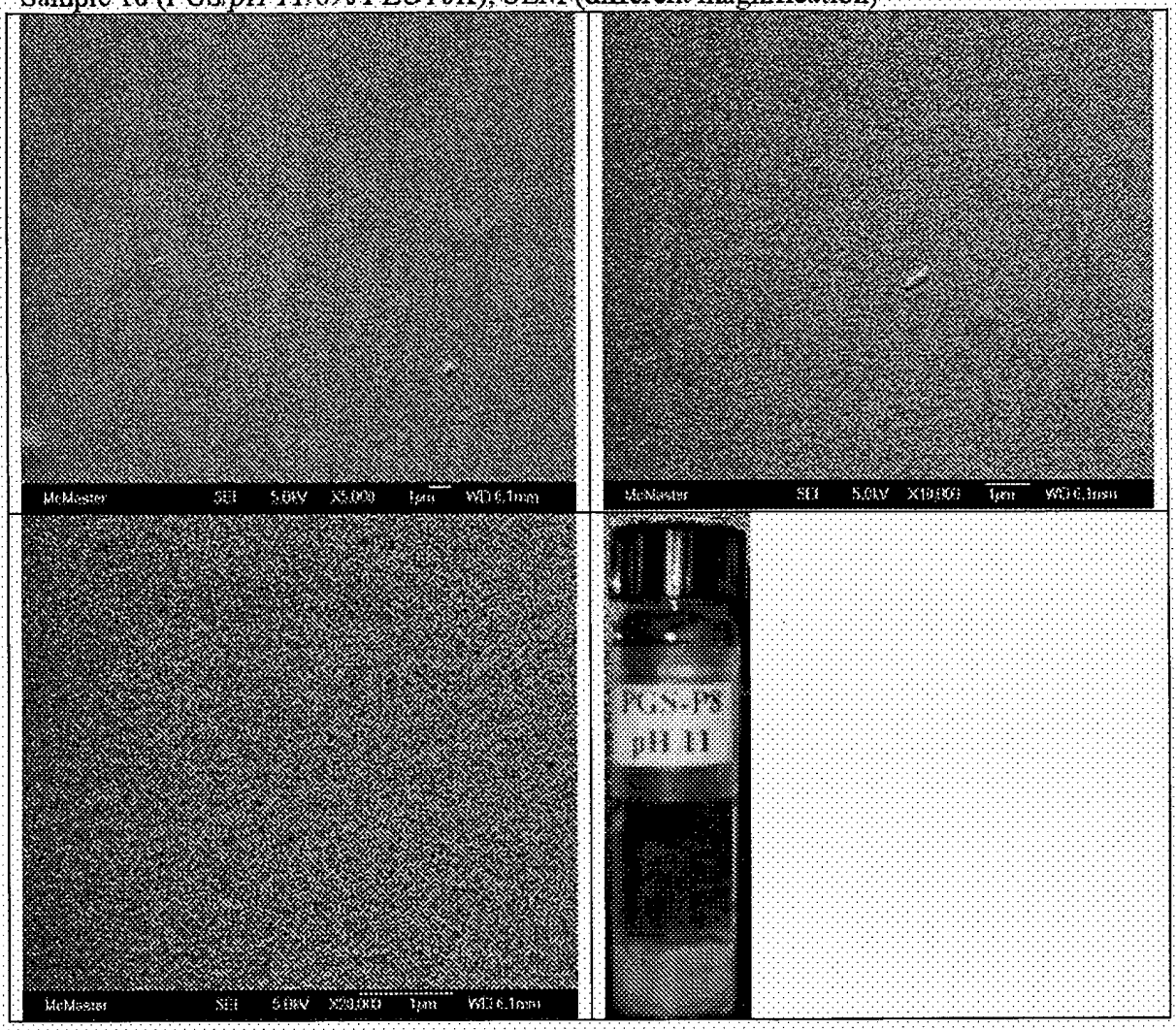
Sample 8 (*TEOS/pH 11/1 eq. glycerol/8% PEO10K*)
Two layer solution, SEM not available



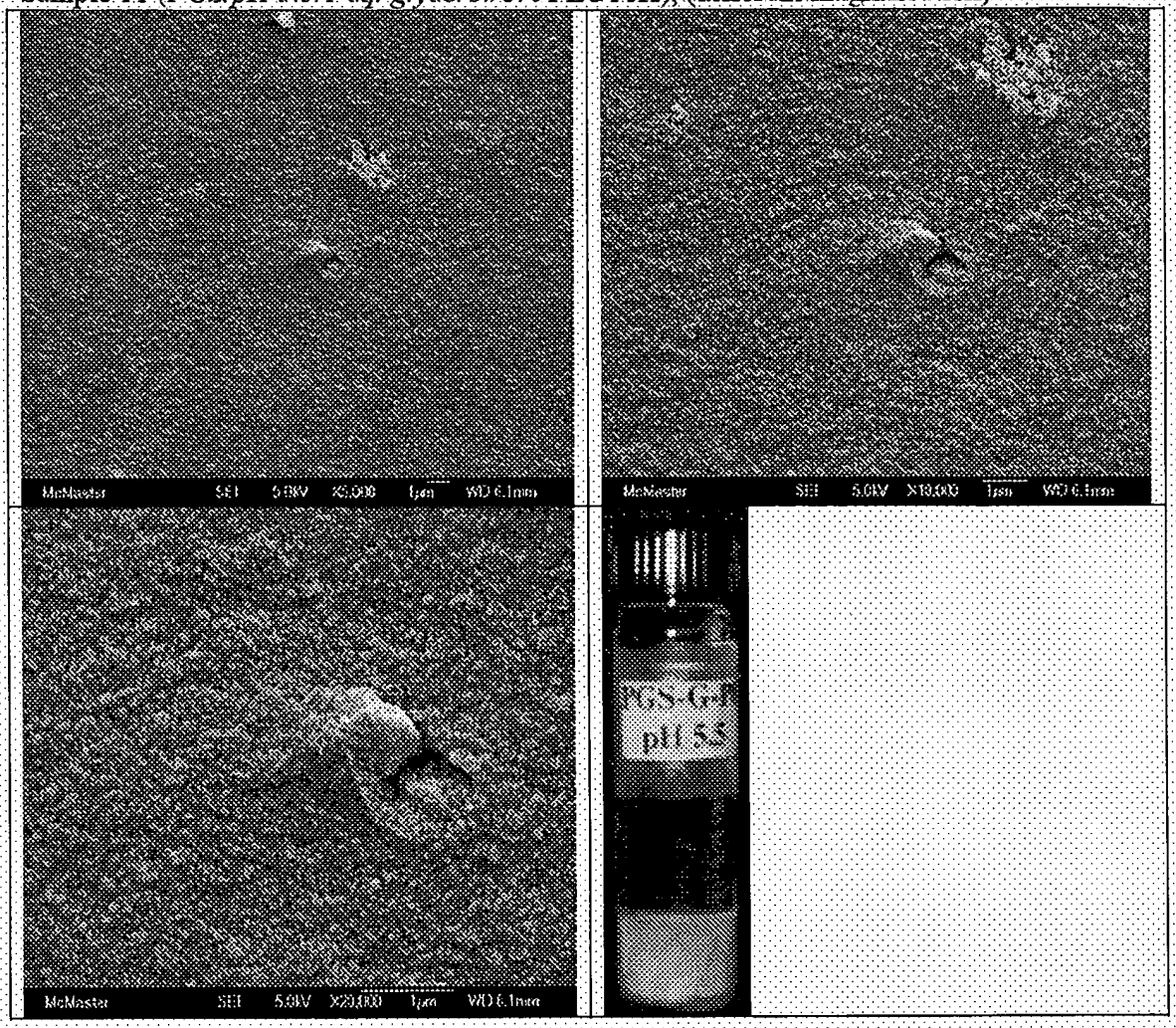
Sample 9 (*PGS/pH 5.5/8% PEO10K*), (different magnification)



Sample 10 (*PGS/pH 11/8% PEO10K*), SEM (different magnification)



Sample 11 (*PGS/pH 5.5/1 eq. glycerol/8% PEO10K*), (different magnification)



Sample 12 (*PGS/pH 11/1 eq. glycerol/8% PEO10K*), (different magnification)